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*Professional paper*

# URINARY TRACT INFECTIONS AND TOTAL PROSTATE SPECIFIC ANTIGEN TPSA

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**Abstract**

**Introduction:** The urinary system consists of four main organs: the kidneys, ureters, bladder, and urethra, and these organs work to filter blood, remove waste, form urine, and eliminate urine from the body. In recent years there have been encouraging strides in understanding and studying the pathogenesis of urinary tract infections (UTIs) and total prostate specific antigen-TPSA.
**Purpose of the study:** The purpose of the research will focus on biochemical markers such as: urea, creatinine, uric acid as urine degradation products and identification of parameters of diseases of the urogenital tract.
Urinary status parameters will also be analyzed such as: proteinuria, hematuria, glycosuria, bilirubin, urobilinogen, pH, etc., parameters which are present during diseases and infections of the urogenital tract.
The purpose of the paper will also analyze the bacteriological and virological parameters such as: ureoplasma, mycoplasma, chlamydia, toxoplasma and cytomegalovirus, which are identifying parameters for infections of the urogenital tract in different age groups and genders.
This work will also consist in the measurement of total prostate specific antigen-TPSA as a main marker for the identification of prostate diseases.
**Material and method:** In the research, a total of 50 male patients will be taken to analyze the urinary condition. Urine analyzes will be performed by collecting urine in sterile cups and using the urine microscopy method and the urine strip test using the chromatographic method, where these analyzes were performed according to the European guideline standards manual (2023).
Vitek is an identification system that can identify bacteria and yeast. This test uses the biochemical reactions and nutrient utilization of the microorganism to make the identification of the bacteria and the antibiogram. The test requires that a sufficient amount of growth be obtained during a specified growth period of 18 – 70 hours.
Patients of the study group for Total Prostate Specific Antigen (TPSA) were analyzed through the blood serum in ng/mL of the patients with the fluorescent immunoassay test method with Vidas Biomerie. Also 20 patients to analyze the total prostate specific antigen TPSA with serum and will be analyzed with fluorescent enzymatic immunoassay methods (Vidas).
SPSS – Software package version 20.0
Numerical series were analyzed using central tendency measures (average, median, minimum values, maximum values), as well as distribution measures (standard deviation);
To determine the regularity of the frequency distribution of the examined variables, the Shapiro-Wilk W Test was used;
Non-parametric tests for two independent parameters were used to test the significance and difference between some numerical parameters with irregular frequency distribution (Mann Whitney U test);
To determine statistical significance, a two-way analysis was used with a significance level (means) of $p<0.05$.
**Results:** From the results, it was found that urinary infections are frequent and appear during the attack with bacteria and viruses such as ureoplasma, mycoplasma, chlamydia and cytomegaloviruses, which are identifying parameters for infections of the urogenital tract in different age groups of the male gender.
**Conclusion:** From the analyzes performed on patients of different age groups, we came to the conclusion that:

- The parameters of the urinary system will be able to give a real picture of infectious diseases of the urinary tract.
- Biochemical markers can identify the functional state of the urinary tract.

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- Antibiogram and cytomegaloviruses - microbiological and virological status can give an insight into the type of urinary infections.
- The prostate-specific antigen TPSA can be taken as the main marker for the identification of tumoral disease of the prostate gland.

*Keywords:* urogenital tract infections, urine, urine parameters, TPSA, tumor diseases.

## 1. Introduction

The renal system consists of two kidneys (where urine is formed) and the conduction system (two ureters, bladder and urethra) that transports and stores urine before it is eliminated from the body. The urinary tract starts from the final part of the collecting ducts of the nephron, to the calyx, which meet in the renal pelvis (pelvis), which continues with the ureters that exit the renal hilus and end in the urinary bladder, which continues with the urethra that excretes the final urine. out. The urinary tract collects the final urine formed in the nephron and passes it down without changing it (Grams ME, Astor BC et al 2010).

The kidneys are two vital excretory organs in the shape of a bean, it has a dark red color, sympathetic innervation (only), with a length of 11–12 cm, a width of 6 cm, a thickness of 2.5 cm (anterior posterior) and a weight of 150 g. The hilus (deepening) of the kidney serves as an entrance site for blood vessels (the kidneys accept about 20-25% of the cardiac output that is used for filtration), lymphatic vessels, nerves, ureters and sinus renalis. The kidneys play a role in filtration, secretion, excretion, regulate the amount of plasma, water and maintain the osmotic balance (through the ions of Na, K, Ca, Cl, phosphates, etc.) and acid-base balance of the blood (through the secretion of hydrogen ions and ammonium formation) (Radhakrishnan J et al., 2014).

Nephrons are the morphological and functional (filtering) units of the kidney (1-3 million nephrons for each kidney). Each nephron consists of a corpuscle (corpusculus) and long tubules (tubes) with closed ends. Each nephron can form its own urine (Bennett JE, et al. 2010).

Urine is fluid secreted by the kidneys, transported by the ureters to the bladder, where it is stored until it is excreted from the bladder through the urethra.

Urinary tract infections (UTIs) are one of the most common infections worldwide. UTIs are associated with a decrease in the quality of life of patients and a significant clinical and economic burden (Ozturk R, et al 2020).

In both community and hospital settings, UTIs pose a threat to public health. They are the most common outpatient infections (Wagenlehner F, et al 2016) and at least half of adult men and women will have more than one UTI in their lifetime (Alos JI, et al 2005).

In healthcare settings, the percentage of patients diagnosed with healthcare-associated UTIs is as high as 9.4% (Tandogdu Z, et al 2016).

UTIs are heterogeneous with regard to their etiology, clinical manifestations, and disease course, which range from simple (e.g., urethritis and cystitis) to severe (e.g., pyelonephritis, bacteremia, and septic shock) (Behzadi P, et al 2015).

Furthermore, the pathogenic microorganisms of UTI are various, with significant changes by years and differences by countries or regions (Ahmadi M, et al 2022).

A wide range of virulence factors and multi-drug resistant pathogenic strains are involved in the pathogenicity and resistance of the uropathogenic agents, making it more difficult to manage these complicated infections (Sarshar M, et al 2020), (Hozzari A, et al 2020).

Prostate cancer remains a significant public health problem, since it is the second most common male malignancy and the fifth major cause of death worldwide. It is responsible for 3.8% of all deaths caused by cancer in male population (Bray F, et al 2018).

Although it is prostate-specific rather than disease-specific, serum prostate-specific antigen (PSA), a glycoprotein normally expressed by prostate tissue, has been a marker of choice for early detection and follow up of patients with prostate carcinoma since its discovery in late 1980s. (Stamey TA, et al 1987)

Since increased PSA serum levels can be found in other conditions, such as many benign changes, urinary tract infections, or after the instrumentation, prostate needle biopsy represents a gold standard for the diagnosis of prostate carcinoma (Magi-Galluzzi C, et al 2018).

Despite the findings of different studies indicating that PSA screening can help in early prostate cancer detection, there has been a lot of inconsistency about its clinical appliance as a screening marker, especially in the last decade. Some of the reasons include a high rate of false positive and negative results on needle biopsy and repeated unnecessary biopsy and delayed diagnosis (Yu W, et al 2020).

Screening with serum PSA aims to detect prostate cancer at an early stage in order to enable adequate treatment and to impact overall and disease-specific mortality (Ilic D, et al 2018).

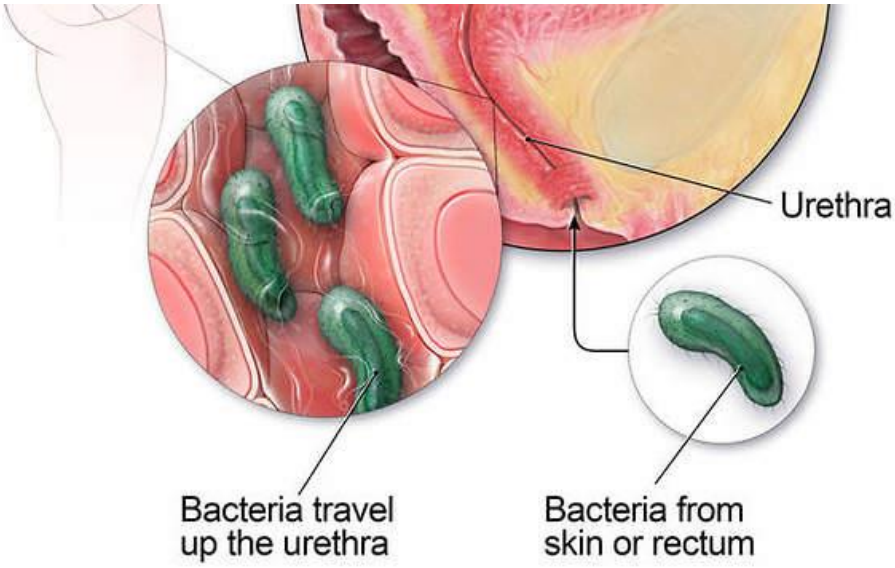



**Figure1. Presentation of UTI in human body** (https://newswire.net/newsroom/pr/00100074-health-experts-explain-the-cause-of-urinary-tract-infections.html)

## 2. Purpose of the study

The purpose of the research will focus on biochemical markers such as: urea, creatinine, uric acid as urine degradation products and identification of parameters of diseases of the urogenital tract.

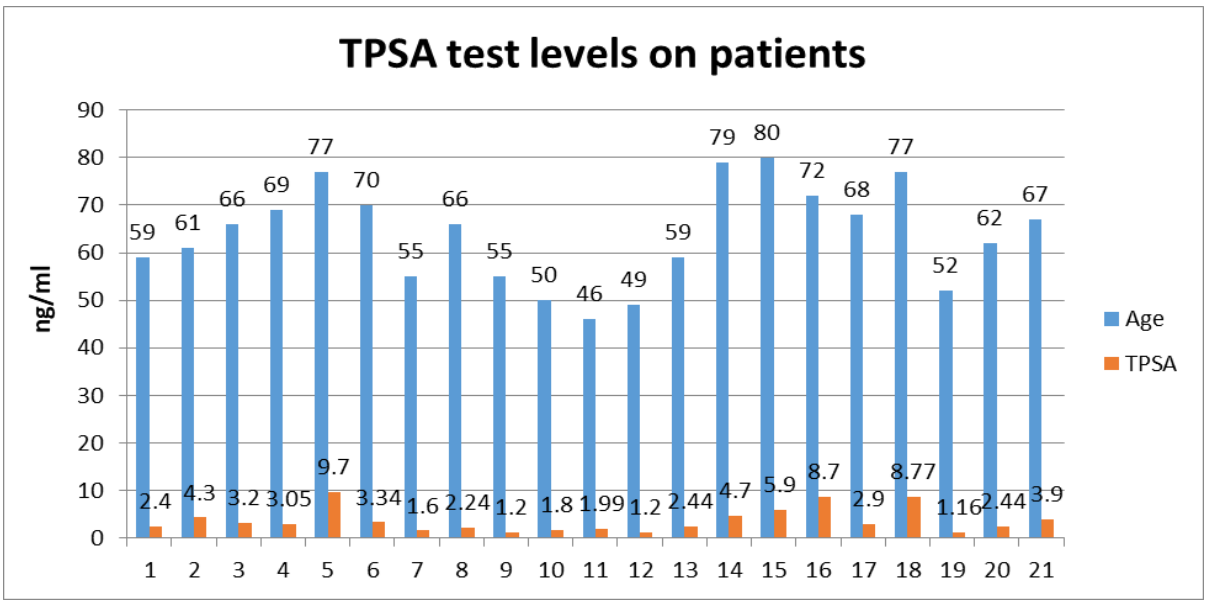
Urinary status parameters will also be analyzed such as: proteinuria, hematuria, glucosuria, bilirubin, urobilinogen, pH, etc., parameters which are present during diseases and infections of the urogenital tract. The purpose of the paper is also to analyze the bacteriological and virological parameters such as: ureoplasma, mycoplasma, chlamydia, toxoplasma and cytomegalovirus, which are identifying parameters for infections of the urogenital tract in different age groups and genders. This work will also consist in the measurement of total prostate specific antigen-TPSA as a main marker for the identification of prostate diseases.

## 3. Material and method

In the research, a total of 50 male patients will be taken to analyze the urinary condition. Urine analyzes will be performed by collecting urine in sterile cups and using the urine microscopy method and the urine strip test using the chromatographic method, where these analyzes were performed according to the European guideline standards manual (2023).
Vitek is an identification system that can identify bacteria and yeast. This test uses the biochemical reactions and nutrient utilization of the microorganism to make the identification of the bacteria and the antibiogram. The test requires that a sufficient amount of growth be obtained during a specified growth period of 18–70 hours.
Patients of the study group for Total Prostate Specific Antigen (TPSA) were analyzed through the blood serum in ng/mL of the patients with the fluorescent immunoassay test method with Vidas Biomerie. Also 20 patients to analyze the total prostate specific antigen TPSA with serum and will be analyzed with fluorescent enzymatic immunoassay methods (Vidas).

## 4. Results

Urine analyzes are the main bioindicators in acute and chronic urinary infections in the identification of bacteria in gram-positive and gram-negative in the urine sediment. Based on the results obtained from the analyzes performed on the patients urine, we have presented the graphics below.



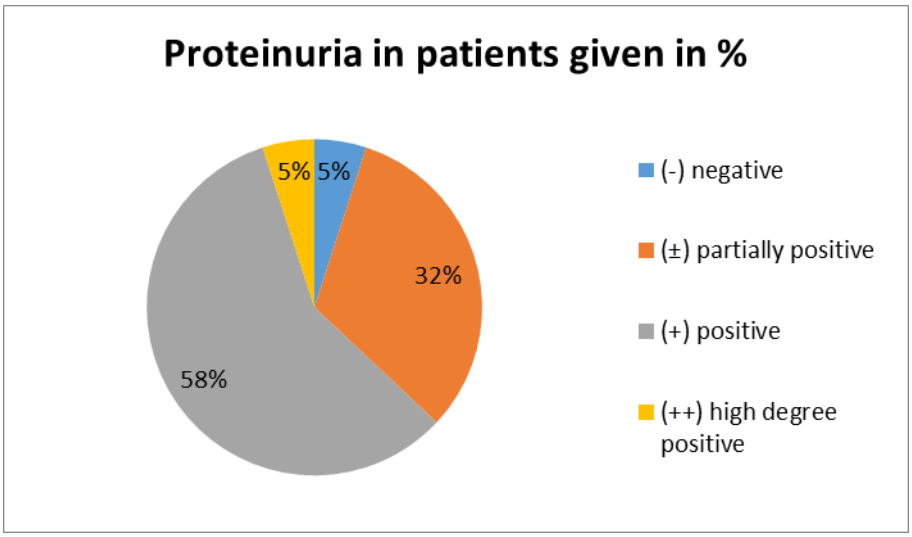

**Graph.1:** TPSA test levels on male patients.

In the graphic above, we notice the values of the prostate specific antigen test in correlation with the age of the patients, where we can clearly see that the older the patients are the higher risk of presenting prostate diseases in correlation with urinoinfection than the control group of analyzed patient.

**Table.1:** Proteinuria in urine sediment of male patients given in percent.

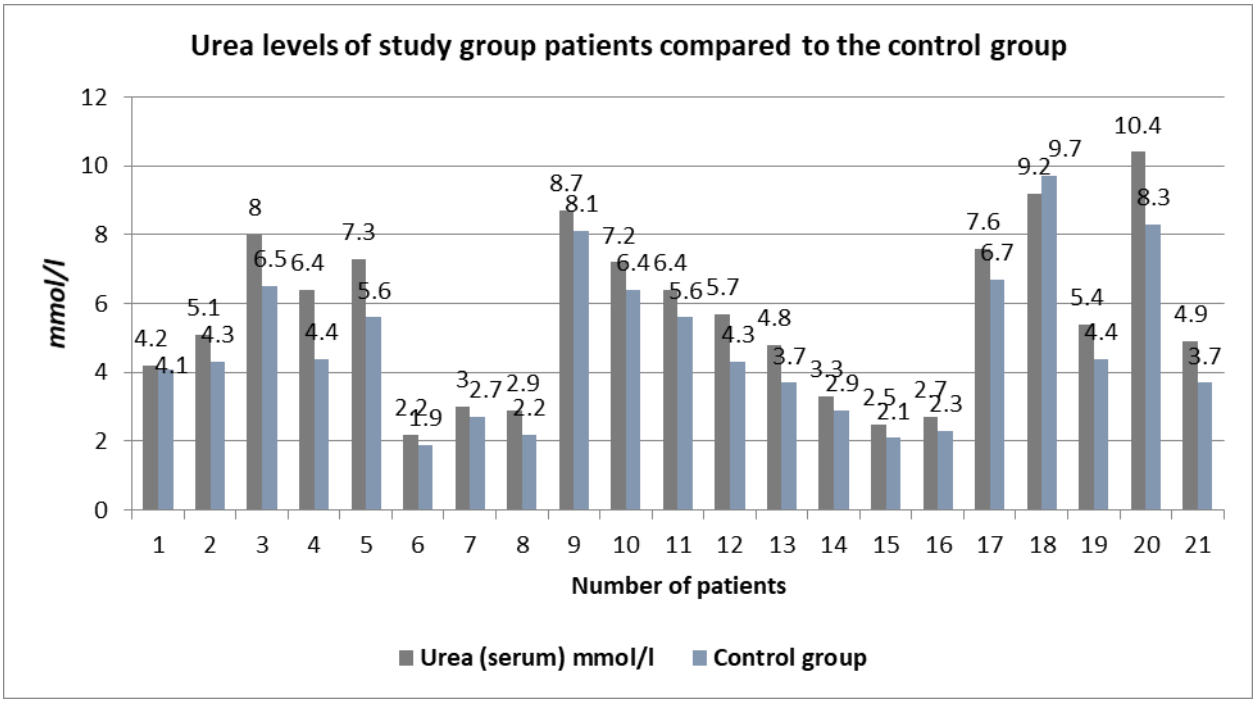
| Proteinuria in urine sediment | Given in percentage |
|---|---|
| (-) negative | 5% |
| (±) partially infection | 32% |
| (+) positive | 58% |
| (++) high degree positive | 5% |

In the table above we have presented the values in percent of proteinuria in urine sediment of patients from different age groups. Patients with partial proteinuria (±) are 32%, with positive proteinuria (+) we have 58% of the analyzed patients and with proteinuria with two pluses(++) and higher(+++) we have 5% of the patients.



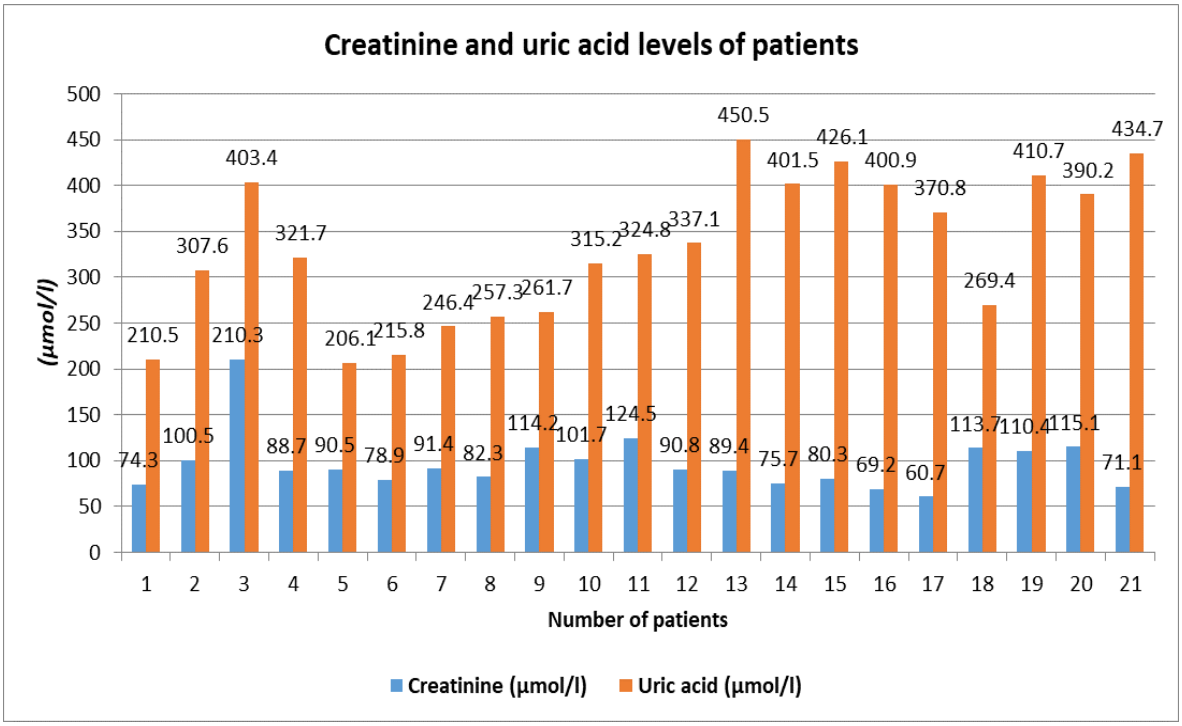

**Graph.2:** Proteinuria in patients given in percent in a scheme pie chart model.

The graphic above presents the occurrence of proteinuria in patients in different age groups. In the graphic we see the percentage where 58% of patients show positive proteinuria (+) in urine sediment, 32% are patients with partial proteinuria (±) in the urine sediment, 5% are negative (-) which means there are no proteins or other intermediate products or cells in the urine sediment and 5% also are patients with high degree positive proteinuria (++) which it means in their urine sediment we have a mass of leucocytes and a mass of erythrocytes as well.




**Graph.3:** Urea levels of study group patients compared to the control group.

The results presented in the graphic show a significant correlation between patients with proteinuria and urea values of the same patients compared to control group.




**Graph.4:** Creatinine and uric acid levels of male patients.

The presence of proteinuria and elements in the urine sediment show a correlation with the uric acid and creatinine of the same patients compared to the patients of the control group.

## 5. Discussion

Urinary tract infections (UTIs) are one of the most common infections worldwide, but little is known about their global scale and long-term trends (Xiaorong Yang et al., 2022).
In both community and hospital settings, UTIs pose a threat to public health. They are the most common outpatient infections, (Wagenlehner F et al., 2016) and at least half of adult women will have more than one UTI in their lifetime (Alos JI. 2005).
UTIs are one of the most frequently diagnosed infections in older adults (Rowe TA et al., 2013). They are responsible for 15 to 30% of all infections in this age group and also contribute to deaths and morbidities (Abrams P et al., 2010).
Bacteria are the most common etiology of UTIs, accounting for more than 95% of cases. E. coli is the most common causal organism of UTIs and is responsible for more than 80% of them (Nachimuthu R et al., 2008).
Wright et al. reported that the rate of E. coli in urine cultures was 67% (Wright SW et al., 1999). Another study conducted by Akbas et al. revealed that the rate of E. coli in urine cultures was 35-80% (Akbas E et al., 1997).
Klebsiella pneumonia is the most relevant human pathogen within genus Klebsiella, causing many infections in hospitals, long-term care facilities and communities worldwide, including lung, urinary tract, abdominal cavity, surgical sites and soft tissues infections, even bacteremia (Mody L et al., 2014) (Shon AS et al., 2013).
Klebsiella pneumoniae strains isolated from urine in UTI patients with CKD are the most important uropathogenic microorganisms, after Escherichia coli. UTIs due to K. pneumoniae are favored by the presence of CKD, with increased blood urea, in turn the CKD evolution to the final stages is accelerated by UTI. Although the percentage of urinary infections with K. pneumoniae is reduced in the case of uropathogenic isolates from patients with advanced CKD stages, isolated strains are multiresistant in more than four classes of antibiotics. The treatment of UTIs caused by K. pneumoniae with trimethoprim/ sulfamethoxazol, nitrofurantoin, first generation of cephalosporins, and even the combination of broad spectrum penicillin (amoxicillin) with beta-lactamase inhibitor (clavulanic acid) has no more favorable effect on patients with UTIs and CKD, due to high resistance (Oanamariana Cristea et al., 2017).

## 6. Conclusion

The total specific antigen of the prostate is one of the main bioindicators of the prostate in men at different age groups, from which then males come to develop acute and chronic urinary infections.
The results of the analyzes of the patients are in correlation with the urine and urinary infections and the analyzes of the total prostate specific antigen show a significance between these two parameters.
The occurrence of proteinuria in patients in different age groups we see the percentage where 58% of patients show positive proteinuria (+) present in urine sediment, 32% are partially positive (±) in the urine sediment, 5% are negative (-) which means there are no proteins or other intermediate products or cells in the urine sediment and 5% also are patients with high degree positive proteinuria (++) which it means in their urine sediment we have a mass of leucocytes and a mass of erythrocytes as well in analyzed patient in correlation with control group.
The results obtained by the patients for urea, creatinine and uric acid show a positive correlation in the patients who have urinary infections and proteinuria compared to the patients of the control group.

The values of the total prostate specific antigen test in correlation with the age of the patients, where we can clearly see that the older the patients are the higher risk of presenting prostate diseases in correlation with urine infection.
Based on the obtained results, we come to the conclusion that every male patient after the age of 50 should do prostate tests and urine tests, which are presented with a high frequency of acute and chronic infections.

## References


[1] Abrams P, Andersson KE, Birder L, Brubaker L, Cardozo L, Chapple C, Cottenden A, Davila W, de Ridder D, Dmochowski R, Drake M, Dubeau C, Fry C, Hanno P, Smith JH, Herschorn S, Hosker G, Kelleher C, Koelbl H, Khoury S, Madoff R, Milsom I, Moore K, Newman D, Nitti V, Norton C, Nygaard I, Payne C, Smith A, Staskin D, Tekgul S, Thuroff J, Tubaro A, Vodusek D, Wein A, Wyndaele JJ; Members of Committees; Fourth International Consultation on Incontinence. Fourth International Consultation on Incontinence Recommendations of the International Scientific Committee: Evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn. 2010;29(1):213-40. doi: 10.1002/nau.20870. PMID: 20025020.

[2] Ahmadi M, Ranjbar R, Behzadi P, Mohammadian T. Virulence factors, antibiotic resistance patterns, and molecular types of clinical isolates of Klebsiella Pneumoniae. Expert Rev Anti Infect Ther. 2022 Mar;20(3):463-472. doi: 10.1080/14787210.2022.1990040. Epub 2021 Oct 28. PMID: 34612762.

[3] Akbas E, Zarakolu P, Aktepe OC, et al. !drar yolu enfeksiyonu ön tanısı ile basvuran olgularda idrar örneklerinin mikrobiyolojik olarak degerlendirilmesi: !ki yıllık bir çalısma. Mikrobiyoloji Bülteni. 1997; 31:351.

[4] Alós JI. Epidemiología y etiología de la infección urinaria comunitaria. Sensibilidad antimicrobiana de los principales patógenos y significado clínico de la resistencia [Epidemiology and etiology of urinary tract infections in the community. Antimicrobial susceptibility of the main pathogens and clinical significance of resistance]. Enferm Infecc Microbiol Clin. 2005 Dec;23 Suppl 4:3-8. Spanish. doi: 10.1157/13091442. PMID: 16854352.

[5] BEHZADI, Payam & Behzadi, Elham & Ranjbar, Reza. (2015). Urinary tract infections and Candida albicans. Central European Journal of Urology. 68. 96-101. 10.5173/ceju.2015.01.474.

[6] Zumla A. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Lancet Infect Dis. 2010 May;10(5):303–4. doi: 10.1016/S1473-3099(10)70089-X. Epub 2010 Apr 21. PMCID: PMC7128814.

[7] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4. PMID: 33538338.

[8] Grams ME, Astor BC, Bash LD, Matsushita K, Wang Y, Coresh J. Albuminuria and estimated glomerular filtration rate independently associate with acute kidney injury. J Am Soc Nephrol. 2010 Oct;21(10):1757-64. doi: 10.1681/ASN.2010010128. Epub 2010 Jul 29. PMID: 20671214; PMCID: PMC3013549.

[9] Hozzari A, Behzadi P, Kerishchi Khiabani P, Sholeh M, Sabokroo N. Clinical cases, drug resistance, and virulence genes profiling in Uropathogenic Escherichia coli. J Appl Genet. 2020 May;61(2):265-273. doi: 10.1007/s13353-020-00542-y. Epub 2020 Jan 16. PMID: 31950434.

[10] Ilic D, Djulbegovic M, Jung JH, Hwang EC, Zhou Q, Cleves A, Agoritsas T, Dahm P. Prostate cancer screening with prostate-specific antigen (PSA) test: a systematic review and meta-analysis. BMJ. 2018 Sep 5;362:k3519. doi: 10.1136/bmj.k3519. PMID: 30185521; PMCID: PMC6283370.

[11] Magi-Galluzzi C. Prostate cancer: diagnostic criteria and role of immunohistochemistry. Mod Pathol. 2018 Jan;31(S1):S12-21. doi: 10.1038/modpathol.2017.139. PMID: 29297490.

[12] Michael Kwok, Guideline of guidelines: management of recurrent urinary tract infections in women, 2022 BJU

[13] Mody L, Juthani-Mehta M. Urinary tract infections in older women: a clinical review. JAMA. 2014 Feb 26;311(8):844-54. doi: 10.1001/jama.2014.303. PMID: 24570248; PMCID: PMC4194886.

[14] Nachimuthu, Ramesh. (2008). Urinary Tract Infection and Antimicrobial Susceptibility Pattern of Extended Spectrum of Beta Lactamase Producing Clinical Isolates. Advances in Biological Research.

[15] Cristea OM, Avrămescu CS, Bălăşoiu M, Popescu FD, Popescu F, Amzoiu MO. Urinary tract infection with Klebsiella pneumoniae in Patients with Chronic Kidney Disease. Curr Health Sci J. 2017 Apr-Jun;43(2):137-148. doi: 10.12865/CHSJ.43.02.06. Epub 2017 Jun 29. PMID: 30595869; PMCID: PMC6284181.
[16] Yang X, Chen H, Zheng Y, Qu S, Wang H, Yi F. Disease burden and long-term trends of urinary tract infections: A worldwide report. Front Public Health. 2022 Jul 27;10:888205. doi: 10.3389/fpubh.2022.888205. PMID: 35968451; PMCID: PMC9363895.
[17] Radhakrishnan J, Remuzzi G, Saran R, Williams DE, Rios-Burrows N, Powe N; CDC-CKD Surveillance Team; Brück K, Wanner C, Stel VS; European CKD Burden Consortium; Venuthurupalli SK, Hoy WE, Healy HG, Salisbury A, Fassett RG; CKD.QLD group; O'Donoghue D, Roderick P, Matsuo S, Hishida A, Imai E, Iimuro S. Taming the chronic kidney disease epidemic: a global view of surveillance efforts. Kidney Int. 2014 Aug;86(2):246-50. doi: 10.1038/ki.2014.190. Epub 2014 Jun 4. PMID: 24897034; PMCID: PMC4593485.
[18] Rowe TA, Juthani-Mehta M. Urinary tract infection in older adults. Aging health. 2013 Oct;9(5):10.2217/ahe.13.38. doi: 10.2217/ahe.13.38. PMID: 24391677; PMCID: PMC3878051.
[19] Sarshar M, Behzadi P, Ambrosi C, Zagaglia C, Palamara AT, Scribano D. FimH and Anti-Adhesive Therapeutics: A Disarming Strategy Against Uropathogens. Antibiotics (Basel). 2020 Jul 10;9(7):397. doi: 10.3390/antibiotics9070397. PMID: 32664222; PMCID: PMC7400442.
[20] Shon AS, Bajwa RP, Russo TA. Hypervirulent (hypermucoviscous) Klebsiella pneumoniae: a new and dangerous breed. Virulence. 2013 Feb 15;4(2):107-18. doi: 10.4161/viru.22718. Epub 2013 Jan 9. PMID: 23302790; PMCID: PMC3654609.
[21] Stamey TA, Yang N, Hay AR, McNeal JE, Freiha FS, Redwine E. Prostate-specific antigen as a serum marker for adenocarcinoma of the prostate. N Engl J Med. 1987 Oct 8;317(15):909-16. doi: 10.1056/NEJM198710083171501. PMID: 2442609.
[22] Tandogdu Z, Wagenlehner FM. Global epidemiology of urinary tract infections. Curr Opin Infect Dis. 2016 Feb;29(1):73-9. doi: 10.1097/QCO.0000000000000228. PMID: 26694621.
[23] Wagenlehner F, Tandogdu Z, Bartoletti R, Cai T, Cek M, Kulchavenya E, Köves B, Naber K, Perepanova T, Tenke P, Wullt B, Bogenhard F, Johansen TE. The Global Prevalence of Infections in Urology Study: A Long-Term, Worldwide Surveillance Study on Urological Infections. Pathogens. 2016 Jan 19;5(1):10. doi: 10.3390/pathogens5010010. PMID: 26797640; PMCID: PMC4810131.
[24] Wright SW, Wrenn KD, Haynes ML. Trimethoprim-sulfamethoxazole resistance among urinary coliform isolates. J Gen Intern Med. 1999 Oct;14(10):606-9. doi: 10.1046/j.1525-1497.1999.10128.x. PMID: 10571705; PMCID: PMC1496756.
[25] Yang X, Chen H, Zheng Y, Qu S, Wang H, Yi F. Disease burden and long-term trends of urinary tract infections: A worldwide report. Front Public Health. 2022 Jul 27;10:888205. doi: 10.3389/fpubh.2022.888205. PMID: 35968451; PMCID: PMC9363895.
[26] Yu W, Zhou L. Early Diagnosis of Prostate Cancer from the Perspective of Chinese Physicians. J Cancer. 2020 Mar 5;11(11):3264-3273. doi: 10.7150/jca.36697. PMID: 32231732; PMCID: PMC7097943.